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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Application Number: 10/045,510
Filing Date: October 19, 2001
Appellant(s): DOLITZKY ET AL.

John B. Starr, Jr.

For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 2/6/2006 appealing from the Office action mailed 12/28/2004.

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

| | | |
|---|---|---|
| WO 00/32555 | JERUSSI et al | 6-2000 |

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-2 and 95-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jerussi et al (WO 00/32555).

The claimed invention is drawn to white crystals of venlafaxine and venlafaxine in a purity of greater than 99.3%. The prior art generally teaches that venlafaxine is a well-known compound useful for treating depression. Applicants acknowledge that the compound is known. See page 1, last paragraph of the specification.

Jerussi et al on page 23 disclosed venlafaxine. The purity appears to be less than what is presently claimed and the color is not white. Jerussi et al taught a "pale yellow solid". Therefore, the prior art differs by not teaching the same purity of the claimed compound and the same color. The difference in purity is that of 99.3%[1] versus an unknown purify compound in Jerussi et al. The difference in color is from a pale yellow solid as shown in Jerussi et al to a white solid as instantly claimed. An ordinary artisan would correlate the color to the purity of the compound. Please note that on page 23 lines 15-27 Jerussi et al actually taught the removal of pink in the making of the pale yellow solid venlafaxine. The final color of the compound is an inherent property pure venlafaxine. An ordinary skilled artisan generally would expect pure compounds to be white.

These differences are not patentable. It would have been obvious to one having ordinary skill in the art at the time application was made to have used well-known techniques of purification, in order to make a very pure composition of venlafaxine. One skilled in the art would be motivated to make a very pure composition of venlafaxine to eliminate the possibility of side effects that might be associated with the impurities. Furthermore, it has been well

[1] See claim 2.

established that the mere purity of compound, in itself, does not render a substance unobvious Ex parte Gray (BPAI 1989) 10 PQ2D 1922.

Claims 95-98 are directed to the same crystals but include process steps M.P.E.P. 2113 states the following:

> *"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).*

The examiner's rationale for why claims 1-2 are obvious also renders obvious claims 95-98. These claims are simply directed to a purer form of a well-known pharmaceutical compound. Purifying this well-known pharmaceutical is obvious for reasons already stated.

**(10) Response to Argument**

A) Response to Applicant's Argument under the heading, "***2. Proper Application of the Prescript of M.P.E.P. § 2144.04 VII that Mere Purity Does Not Render Patentable a Purer Form of a Known Compound Requires that the Purity be Construed as General Purity.***"

Applicant presents some general points on how the term "purity" should be construed. Applicant concludes that "purity" should be construed in the sense of "general purity" or assay.

The examiner doesn't find this argument persuasive. When construing the claims, one must look at the art as a whole. In this case, the compound is a known "pharmaceutical drug".

Purity in the pharmaceutical art would clearly not be a "general purity". Venlafaxine is a well-known compound useful for treating depression. One of ordinary skill in the pharmaceutical art would fundamentally be motivated to purify an active compound in order to determine the source of the different side effects that might be associated with the compound and its impurities. The observed side effects often times are attributable to impurities or even to one of the enantiomers. Therefore, skilled artisans routinely purify these pharmaceutically active compounds in order to have a better understanding of the desired and undesired effects associated with the compounds. This desired qualitative analysis means that skilled artisans in this art would use the most advance techniques in obtaining a pure final compound.

Furthermore, the trend before the FDA is toward optically resolving pharmaceutical compounds with an expectation of reducing the side effects. Optically active compounds are extremely pure. Therefore, it is clear that one skilled in the art would be motivated to have an extremely pure compound of venlafaxine. One skilled in the pharmaceutical art thus would clearly be motivated to use standard crystallization techniques in order to isolate a pure compound. Moreover, one skilled in art would possibly be required by the FDA to provide as pure as compound as possible in order to determine the source of possible side effects.

Applicant's reliance of *Sponnoble*[2] misses the mark. There is no evidence that the claimed white crystals of venlafaxine overcome a known problem associated with this compound. As stated above, because venlafaxine was a known drug used to treat depression,

[2] Sponnable, 405 F.2d 578, 585 (C.C.P.A. 1969); See page 7 of applicant's brief.

one skilled in the art would be motivated to purify the compound in order to possibly minimize side effects. The "purity" is important not the "color". If one should find that the 100% pure compound of venlafaxine is purple is would not negate the fact that there was strong motivation in the art to purify venlafaxine. The color purple would not make it a better anti-depressant.

The examiner is aware that color may have more patentable weight in some art areas. For example, the art area where monomers are used to make polymers, color in the monomer can be a major factor in controlling the color of the final product made. The color of a polymer is considered a substantially feature of that polymer. But, in this case, venlafaxine is a well-known pharmaceutical compound. Thus a strong incentive exists to purify the compound regardless of the color.

B) Response to Applicant's Argument under the heading; "***3. The Office Erroneously Equates Color and General Purity or Assay.***"

Applicants submit that the examiner incorrectly correlated color and purity. To support their position applicants present arguments pertinent to "sapphires and rubies". Applicants' arguments are directed to a completely different art area. This is a completely non-analogous art area. These are gems. Applicant is reminded that venlafaxine was a known compound with a known utility. Thus these arguments are neither relevant nor convincing.

Applicants also submit, as evidence, that an impurity component in paroxetine hydrochloride may be responsible for exhibiting a pink color. Applicants argue that there was great difficultly in removing this pink color. This argument is not convincing because as stated by applicants this compound is an "ionic liquid" which is not a crystalline compound. Applicants clearly state, "most Ionic Liquids are colorless. Thus again this evidence is not

directed to analogous art. Furthermore, the color "problem" associated with paroxetine hydrochloride is apparently well documented. Thus, the color pink might be evidence for a recognized problem in that art. But stronger evidence would be showing how color affects the utility of the compound. For example, in some polymer art areas, the desirability of color free monomers is well documented.

C) Response to Applicant's Argument under the heading; "***4. Crystallinity, and Not General Purity or Assay, may dictate a Compound's Color.***"

Applicants submit the proposition that a crystalline structure can exhibit a specific color which is supported with evidence of a compound labeled "ROY". Applicants submit that different polymorphs of the same compound have different colors and thus are correlated with specific crystalline structures.

The examiner does not find, in the record of this case, that color is associated with a specific polymorph. If such evidence did exits it would have been most pertinent. If the white color of venlafaxine clearly indicated a specific polymorph, then the examiner would have found it to be allowable if this polymorph was not known in the prior art. However, in that case the color would have clearly been correlated with a specific polymorph. Polymorphs are known to have different properties. Furthermore, the evidence of "ROY" appears to be unique. There is no general teaching in organic chemistry that even different polymorphs would reasonably be expected to exhibit different color characteristics. If the whiteness of the instant claimed compound is correlated with some specific property it is applicant's burden to provide such evidence. The color in organic compounds will be prima facie an inherent property of the

compound itself. Crystalline color is no different than claiming a compound with a specific melting point, density or any other property of the compound.

This evidence fails to rebut the examiners position that one of ordinary skill in the art would reasonably know that:

1) Crystallization is a well-known purity process because when a solution is allowed to crystallize slowly, impurities are excluded from the growing crystal structure. The impurities are excluded because the molecules in the crystal lattice are in equilibrium with the molecules in solution and molecules unsuitable for the lattice (impurities) are likely to remain in solution.

2) Choosing an ideal solvent for crystallization and recrystallization is well within the purview of an ordinary artisan. Fundamental principles taught to one taking organic chemistry in choosing a solvent for crystallization are finding a solvent that 1) dissolves a moderately large amount of the compound when hot 2) does not react with the compound 3) boils at temperature below the compound's melting point and 4) dissolves only a small amount of compound when cool. These are some simply well known facts about crystallization.

D) Response to Applicant's Argument under the heading; "***B. A Stable White Crystalline Material is not Prima Facie Obvious over a Yellow Gum that Solidifies upon Standing.***

Applicants submit that *In re Cofer* is on point. However, in applicant's own summary of *In re Cofer*, he states that; "***Appellants pointed to the various advantages of its crystalline product as compared to the prior art such as for example, better color, high epoxy content, lower impurity content, and easier to handle.....***".

In this case, applicant has not clearly provided clear and convincing proof of advantages over the prior art. Moreover, in *Cofer* the claimed compound was known to be useful in the

preparation of thermosetting epoxy resins[3]. This is a different art area than pharmaceutical compounds. Color consideration in the resin art can be an important consideration because there is no overwhelming requirement to make ultra pure compounds. Moreover, the claims in *Cofer* were directed to "free-flowing crystals of 2, 2-bis (2, 3-epoxypropoxyphenyl) propane" not to the color of the compound. In the resin art the flowability can be a highly desired featured.

The instant claims are directed to the pharmaceutical art which has a different desirability. An ordinary artisan will be highly motivated, if not absolutely required, to produce a compound useful as a drug in a highly pure form. A skilled artisan would use all of his standard skill sets in order to make the compound pure. One well-known technique is crystallization. Absent some evidence that there was a long felt need for a highly pure venlafaxine and that skilled artisans were unsuccessful in their attempts to make said venlafaxine, it would have been prima facie obvious to an ordinary skilled artisan in the pharmaceutical art to make a pure form of the compound. If evidence was submitted that clearly indicated that skilled artisans made numerous attempts to make pure venlafaxine but were unsuccessful, it would have been most pertinent to the patentably consideration of the claimed crystals. However, no such evidence was submitted.

Ironically when applicants submit alleged advantages of the claimed white crystal of venlafaxine they state the following; **" Applicants are the first to have successfully produced venlafaxine as a white crystalline solid, which , like the 2,2,-B in *Cofer* but especially in view of its use in pharmaceutical, provides significant advantages in color, form and *purity*."** Thus, applicant himself correlates the "whiteness" of the compound with "purity". In

[3] See In re Cofer, first paragraph after claims.

the pharmaceutical art the examiner is clearly aware why a pure compound is highly desired. As stated earlier, the side effects associated with a drug composition can be associated with an impurity or even an optical isomer. However, the examiner is unaware how the color of the compound in the pharmaceutical art is important to its utility.

E) Response to Applicant's Arguments under the heading; "***C. The '555 Publication Teaches Away form a White Crystalline Form and the Obviousness Rejection is Improperly Based on Hindsight.***"

Applicants submit that the '555 reference teaches venlafaxine as a yellow gum thus would discourage the skilled artisan from attempting to obtain a crystalline solid. This argument is not convincing because a skilled artisan's knowledge would not be limited to what is disclosed in the '555 publication. A skilled artisan in the pharmaceutical art would clearly have been motivated to make pure venlafaxine for reasons already stated. Moreover, '555 taught venlafaxine as a pale yellow solid which is not a gum. One of ordinary skill in the art with a pale yellow solid would attempt to further purify this compound by what methods? Obviously as done by even students taken organic chemistry, they would recrystallize the yellow solid in the appropriate solvents. If evidence was submitted that clearly indicated that skilled artisans had made numerous attempts to make pure venlafaxine but were unsuccessful, it would have been most pertinent to the patentably consideration of the claimed crystals. However, no such evidence was submitted.

F) Response to Applicant's Arguments under the heading; "***D. The Examiner has Improperly Taken Official Notice by Equating Color with Purity.***

Applicants submit that the Examiner has failed to provide evidence that correlates purity of a compound with white crystals. Applicants submit that the examiner has taken judicial notice in his assessment that the pure crystals would be expected to be white. These arguments are not convincing. The examiner position is as follows:

a) One with ordinary skill in the art would be motivated to make a pure pharmaceutical compound using all the techniques available to them. Please note that applicant did not contest the examiner reasons as to why would be motivated to obtain a pure pharmaceutical compound. Applicant's rebuttal is silent to the Examiner's position that one skilled in the art would have been motivated to purify the venlafaxine with crystallization, but instead attempts to highlight the color aspect of the claimed compound. As stated earlier, a skilled artisan in the pharmaceutical art would be motivated to obtain a pure compound for safety reasons not for color factors. Therefore, even if a compound were found to have a unique color in the pure form it would be of little importance to one of skilled in the pharmaceutical art. Even the general public when taking medicaments wants them to pure as possible. It is fundamental known that side effects are associated with every pharmaceutical drug. It is fundamentally known that pharmaceutical drugs are characterized for possible side effects and the characterization of these drugs are preferred to be done on very pure compounds. This characterization of side effects is done even on the polymorph level. With these well-known facts, it is without doubt clear that one skilled in the art would be motivated to make pure venlafaxine.

b) Even though color in a compound doesn't always indicate impurity, it is a basic fundamental principle taught to those taking organic chemistry in college, that the appearance of color prima facie indicates the presence of an impurity. Crystallization and recrystallization in

the appropriate solvent in order to purify the compound and the whiteness of the compound usually indicates a level of purity.

c) Even if the color "white" is not always associated with a pure compound, when a skilled artisan purifies a crystalline compound and most impurities are removed, the color of the compound is a property of the compound itself. Even the group of organic compounds which are known to be chromphores[4]the color is a property of the compound. In the pharmaceutical art, the color of the compound has no bearing of the property itself. In other words, a green highly pure compound is no different from a white highly pure compound in the pharmaceutical art.

It is with these facts and rationale that the examiner has relied upon. Applicant's request for a specific reference that teaches one skilled in the art would crystallize a compound in order to obtain a white crystal fails to acknowledge the examiner's true position. Applicants do not rebut the examiner's fundamental statements of facts.

**(11) Related Proceeding(s) Appendix**

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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[4] A chemical group capable of selective light absorption resulting in the coloration of certain organic compounds